IN THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

Claims 1-8 (Cancelled)

9. (Currently Amended) A method of identifying a cDNA encoding a signal sequence, comprising:

directionally introducing a cDNA into a vector, said vector comprising;

a prokaryotic promoter, a eukaryotic promoter, a multiple cloning site, and a nucleic acid encoding a leaderless secretable selection protein,

wherein ~~said introducing~~ introduction of the cDNA into the multiple cloning site results in the formation of a cDNA-selection protein fusion protein-encoding nucleic acid operably linked to the prokaryotic promoter and to the eukaryotic promoter;

introducing the vector comprising the fusion nucleic acid into a bacterial cell;

exposing the bacterial cell containing the cDNA to a selection medium;

determining growth of the bacterial cell in said selection medium, wherein growth of the bacterial cells in said selection medium is indicative of a signal sequence encoded in said cDNA;

introducing the vector identified as comprising a cDNA encoding a signal sequence into a eukaryotic ~~cells~~ cell;

culturing the transfected eukaryotic ~~cells~~ cell; and

detecting secretion of the cDNA-selection protein fusion protein in the cell culture;

wherein ~~the vector expresses a fusion protein encoded by the cDNA and the nucleic acid encoding the selection protein~~ detection of secreted cDNA-selection protein fusion protein indicates the cDNA in the vector encodes a signal sequence.

10. (Currently Amended) A method of identifying a cDNA encoding a signal sequence, comprising:

directionally introducing a cDNA into a vector, said vector comprising a prokaryotic promoter, a eukaryotic promoter, a multiple cloning site, and a nucleic acid encoding a leaderless β-lactamase protein, wherein ~~said introducing~~ introduction of the cDNA into the multiple cloning site results in the formation of a ~~cDNA-β-lactamase~~ fusion nucleic acid encoding a cDNA-β-lactamase fusion protein operably linked to the prokaryotic promoter and to the eukaryotic promoter;

introducing the vector comprising the fusion nucleic acid into a bacterial cell;

exposing the bacterial cell to a selection medium;

determining growth of the bacterial cell in said selection medium, wherein growth of the bacterial ~~cells~~ cell in said selection medium is indicative of a signal sequence encoded in said cDNA;

introducing the vector identified as comprising a cDNA encoding a signal sequence into a eukaryotic ~~cells~~ cell;

culturing the ~~transfected~~ eukaryotic ~~cells~~ cell; and

detecting secretion of the ~~cDNA-selection protein~~ cDNA-β-lactamase fusion protein in the cell culture;

wherein ~~the vector expresses a fusion protein encoded by the cDNA and the nucleic acid encoding the selection protein~~ detection of cDNA-β-lactamase fusion protein in the cell culture indicates the cDNA encoding a signal sequence.

11. (Original) The method of claim 10, wherein the selection medium is a medium comprising β-lactam antibiotic.

12. (Original) The method of claim 11, wherein the selection medium is a medium comprises ampicillin.

13. (Original) The method of claim 10, wherein the β-lactamase is detected in cell culture using a nitrocefin hydrolysis assay.

14. (Currently Amended) The method of claim 6 9, wherein the vector comprises a mammalian promoter and a bacterial promoter.

15. (Currently Amended) A method of producing a cDNA library enriched for cDNAs encoding proteins comprising signal sequences, said method comprising:

directionally introducing each of a plurality of cDNAs into a vector, said vector comprising a prokaryotic promoter, a eukaryotic promoter, and a nucleic acid encoding a leaderless secretable selection protein, said introducing providing for production of a cDNA-selection protein fusion protein in a bacterial cell and in eukaryotic cell

introducing each vector into ~~a~~ bacterial ~~cell~~ cells to create a library of bacterial cells comprising the plurality of cDNAs; and

culturing the library of bacterial cells in a selection medium such that cells that express and secrete the cDNA-selection protein fusion protein grow in the selection medium;

~~expressing the cDNAs in the bacterial cells; and~~

~~selecting bacterial cells containing a cDNA encoding a secreted protein by growth in a selection medium;~~

wherein ~~the selected bacterial cells are enriched for proteins comprising signal sequences~~ said culturing produces a cDNA library enriched for cells containing a vector containing a cDNA encoding a signal sequence.

16. (Original) The method of claim 15, wherein the cDNAs are 5' biased.

17. (Currently Amended) The method of claim 15, ~~wherein the bacterial cells are subjected to~~ comprising culturing the cells a second time so as to provide for a second round of selection in a selection medium.

Claims 18-26 (Cancelled)

27. (New) The method of claim 15, further comprising:

introducing the vectors identified as comprising a cDNA encoding a signal sequence into a eukaryotic cell;

culturing the eukaryotic cell; and

detecting secretion of the cDNA-selection protein fusion protein in the eukaryotic cell culture;

wherein detection of secreted cDNA-selection protein fusion protein indicates the cDNA in the vector encodes a signal sequence.

28. (New) The method of claim 9, wherein the leaderless secretable selection protein is β-lactamase.